to 9-mers and 10-mers, "substantial homology." At 14:1-5, the specification quite plainly teaches that this substantial homology can be differing by no more than 20%. For a 10-mer, this recital is unambiguously equivalent to "no more than a total of two single amino acid" alterations. And this particular language is only used in the claims with respect to 10-mers – so explicit support is clearly found in the specification. For the 9-mer recited in some of the claims, 14: 21-25 provides explicit support. Thus, to the extent that the rejection asserts a lack of verbal antecedent in the specification for the recitations, the rejection is in error and should be withdrawn.

Alternatively, the rejection could seek to assert the type of rejection as issue in Regents of the University of California v. Eli Lilly, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997), the case that appears to be a primary inspiration for the Written Description Guidelines. The written description requirement of this type disallows claims to functional concepts that are ungrounded in concrete, identifiable parameters. But the claims do set forth concrete, identifiable parameters. Lilly was about claiming "vertebrate", "mammalian" and "human" cDNA of a certain type, based apparently on an assertion that the applicant provided the tools to really identify these classes of nucleic acids and distinct nucleic acids.

The Lilly court stated that a written description of an invention involving a chemical genus, like a description of a chemical species, "requires a precise definition, *such as by structure, formula [or] chemical name.*" Lilly at 1568. Where there is such a clear formula, as here, the Lilly rejection does not apply. This conclusion follows not just from the Lilly case itself, but from recent explanatory language from the Court of Appeals for the Federal Circuit, in which the court stated:

> Both Eli Lilly and Enzo Biochem are inapposite to this case because the claim terms at issue here are not new or unknown biological materials *that ordinarily skilled artisans would easily miscomprehend.*

Amgen Inc. v. Hoecst Marion Roussel, Inc., 2003 WL 41993, *13 (Fed. Cir. 2003).[2] Thus, the court identifies the critical component of a Lilly type written description rejection: whether one

[2] Copy attached, with cited text at printed page 17.

understands the scope of what is being claimed. Here there is no such ambiguity, and no Lilly issue.

Furthermore, it cannot be proper to maintain a Lilly type written description against a chemical formula case, since, Applicant respectfully submits, each and every issue of the gazette is replete with claims that are just as susceptible to such a rejection as the concrete claims presented here.

If, for an invention defined by formula, there is an issue of scope, the rejection falls under enablement law. In this case, there has already been a rejection for asserted lack of enablement, which has been rebutted and properly has not been maintained.

For the reasons set forth above, Applicant respectfully submits that the rejection should be withdrawn.

Terminal Disclaimer

The claims are rejected for asserted obviousness-type double patenting. A terminal disclaimer is enclosed to obviate this rejection.

Conclusion

In light of the above discussion and amendments, it is respectfully submitted that the claims are in condition for allowance. The issuance of a Notice of Allowance is earnestly solicited.[3]

Respectfully submitted,

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[3] **FEE DEFICIENCY**

IF ANY ADDITIONAL EXTENSION IS REQUIRED, PLEASE CONSIDER THIS PAPER A PETITION FOR SUCH AN EXTENSION; ANY FEE FOR THE EXTENSION REQUIRED FOR CONSIDERATION OF THIS PAPER BUT NOT ENUMERATED ABOVE OR IN A TRANSMITTAL OR OTHER ASSOCIATED PAPER CAN BE CHARGED TO ACCOUNT NO. 04-0480.

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APPENDIX A1: PENDING CLAIMS (CLEAN COPY)

67. (**Amended**) An isolated molecule comprising a polypeptide that induces an hepatitis C virus (HCV)-specific response in cytotoxic T lymphocytes having a sequence that

(a) has no more than a total of two single amino acid substitutions, deletions or insertions at the corresponding amino acid positions in a CTL epitope which is

LLALLSCLTV ($Core_{178-187}$; SEQ ID NO:2),

QLRRHIDLLV ($E1_{257-266}$; SEQ ID NO:3),

KLVALGINAV ($NS3_{1406-1415}$; SEQ ID NO:28), or

LLFNILGGWV ($NS4_{1807-1816}$; SEQ ID NO:35), or

(b) has no more than one single amino acid substitution, deletion or insertion at the corresponding amino acid positions as in a CTL epitope which is

ADLMGYIPLV ($Core_{131-140}$; SEQ ID NO:1),

LLCPAGHAV ($NS3_{1169-1177}$; SEQ ID NO:26), or

SLMAFTAAV ($NS4_{1789-1797}$; SEQ ID NO:34),

wherein said molecule comprises at least eight amino acids and less than 50 amino acids, with the provisos that (i) when said selected CTL epitope is SLMAFTAAV ($NS4_{1789-1797}$; SEQ ID NO:34), then said molecule comprises from at least eight amino acids to less than 25 amino acids, or (ii) when said selected CTL epitope is LLALLSCLTV ($Core_{178-187}$; SEQ ID NO:2) then said molecule comprises at most ten amino acids.

68. (**Unchanged**) The molecule of claim 67, wherein the isolated peptide has less than 20 amino acids.

69. (**Unchanged**) The molecule of claim 67, wherein the isolated peptide has from 8 to 12 amino acids.

APPENDIX A1: PENDING CLAIMS (CLEAN COPY) – (continued)

70. (**Unchanged**) The molecule of claim 67, wherein the isolated peptide has 9 or 10 amino acids.

71. (**Unchanged**) The molecule of claim 67, 68, 69, or 70, wherein the isolated molecule has a sequence that has no more than a total of one amino acid substitution, deletion or insertion at the corresponding position as in LLALLSCLTV ($Core_{178-187}$; SEQ ID NO:2).

72. (**Unchanged**) The molecule of claim 67, 68, 69, or 70, wherein the isolated molecule has a sequence that has no more than a total of one amino acid substitution, deletion or insertion at the corresponding position as in QLRRHIDLLV ($E1_{257-266}$; SEQ ID NO:3).

73. (**Unchanged**) The molecule of claim 67, 68, 69, or 70, wherein the isolated molecule has a sequence that has no more than a total of one amino acid substitution, deletion or insertion at the corresponding position as in KLVALGINAV ($NS3_{1406-1415}$; SEQ ID NO:28).

74. (**Unchanged**) The molecule of claim 67, 68, 69, or 70, wherein the isolated molecule has a sequence that has no more than a total of one amino acid substitution, deletion or insertion at the corresponding position as in LLFNILGGWV ($NS4_{1807-1816}$; SEQ ID NO:35).

75. (**Unchanged**) An immunogenic composition that induces an hepatitis C virus (HCV)-specific response in cytotoxic T lymphocytes (CTL) comprising molecule which comprises a peptide having a sequence that has no more than a total of a total of two amino acid substitutions, deletions or insertions at the corresponding positions as in a CTL epitope which is

ADLMGYIPLV ($Core_{131-140}$; SEQ ID NO:1),

LLALLSCLTV ($Core_{178-187}$; SEQ ID NO:2),

APPENDIX A1: PENDING CLAIMS (CLEAN COPY) – (continued)

QLRRHIDLLV ($E1_{257-266}$; SEQ ID NO:3),

KLVALGINAV ($NS3_{1406-1415}$; SEQ ID NO:28), or

LLFNILGGWV ($NS4_{1807-1816}$; SEQ ID NO:35) or

has no more than a total of one substitution, deletion or insertion at the corresponding amino acid positions as in a CTL epitope which is

LLCPAGHAV ($NS3_{1169-1177}$; SEQ ID NO:26),

SLMAFTAAV ($NS4_{1789-1797}$; SEQ ID NO:34), or

ILDSFDPLV ($NS5_{2252-2260}$; SEQ ID NO:42).

76. **(Unchanged)** The immunogenic composition of claim 75, wherein the immunogenic composition further comprises a label selected from the group consisting of a radioactive label, an enzymatic label, and a fluorescent label.

77. **(Unchanged)** The immunogenic composition of claim 75, wherein the immunogenic composition further comprises a solid matrix.

78. **(Unchanged)** The immunogenic composition of claim 75, wherein the immunogenic composition further comprises a carrier molecule.

79. **(Unchanged)** The immunogenic composition of claim 75, wherein the carrier molecule comprises a protein or an immunogenic lipid.

80. **(Unchanged)** The immunogenic composition of claim 75, wherein the immunogenic composition further comprises a T-helper lymphocyte epitope.

APPENDIX A1: PENDING CLAIMS (CLEAN COPY) – (continued)

81. (**Unchanged**) The immunogenic composition of claim 75, wherein the immunogenic composition further comprises an additional peptide.

82. (**Unchanged**) The immunogenic composition of claim 81, wherein the additional peptide has a sequence that has no more than a total of two amino acid substitutions, deletions or insertions at the corresponding positions as in KLVALGINAV ($NS3_{1406-1415}$; SEQ ID NO:28).

83. (**Unchanged**) A method of stimulating a cytotoxic T-lymphocyte (CTL) response to an hepatitis C viral immunogen, comprising contacting an HLA class I-restricted cytotoxic T lymphocyte with a composition comprising a peptide that induces an hepatitis C virus (HCV)-specific response in cytotoxic T lymphocytes comprising a sequence that has no more than a total of two single amino acid substitutions, deletions or insertions at the corresponding positions as in a CTL epitope which is

ADLMGYIPLV ($Core_{131-140}$; SEQ ID NO:1),
LLALLSCLTV ($Core_{178-187}$; SEQ ID NO:2),
QLRRHIDLLV ($E1_{257-266}$; SEQ ID NO: 3),
KLVALGINAV ($NS3_{1406-1415}$; SEQ ID NO:28), or
LLFNILGGWV ($NS4_{1807-1816}$; SEQ ID NO:35) or

has no more than a total of one single amino acid substitution, deletion or insertion at the corresponding amino acid positions as in a CTL epitope which is

ADLMGYIPLV ($Core_{131-140}$; SEQ ID NO:1),
LLCPAGHAV ($NS3_{1169-1177}$; SEQ ID NO:26),
SLMAFTAAV ($NS4_{1789-1797}$; SEQ ID NO:34), or
ILDSFDPLV ($NS5_{2252-2260}$; SEQ ID NO:42).

APPENDIX A1: PENDING CLAIMS (CLEAN COPY) – (continued)

84. (**Unchanged**) The method of claim 83, wherein the contacting occurs in a mammal.

85. (**Unchanged**) The method of claim 83, wherein the mammal is free of HCV disease, is a carrier of HCV, or is afflicted with HCV disease.

86. (**Unchanged**) The method of claim 83, wherein the contacting occurs *in vitro*.

87. (**Unchanged**) The method of claim 83, wherein the peptide comprises the sequence which is ADLMGYIPLV ($Core_{131-140}$; SEQ ID NO:1).

88. (**Unchanged**) A method of detecting cytotoxic T cells that respond to a T cell epitope of hepatitis C virus (HCV), the method comprising the steps of:

(a) preparing HLA class I-restricted cytotoxic T cells;

(b) preparing HLA class-I matched and -mismatched target cells;

(c) containing separately matched and mismatched target cells with a composition comprising a peptide that induces an HCV-specific response in cytotoxic T lymphocytes having the sequence that has no more than a total of two single amino acid substitutions, deletions or insertions at the corresponding positions as in a CTL epitope which is

ADLMGYIPLV ($Core_{131-140}$; SEQ ID NO:1),

LLALLSCLTV ($Core_{178-187}$; SEQ ID NO:2),

QLRRHIDLLV ($E1_{257-266}$; SEQ ID NO: 3),

KLVALGINAV ($NS3_{1406-1415}$; SEQ ID NO:28), or

LLFNILGGWV ($NS4_{1807-1816}$; SEQ ID NO:35) or

has no more than a total of one single amino acid substitution, deletion or insertion at the corresponding amino acid positions as in a CTL epitope which is

APPENDIX A1: PENDING CLAIMS (CLEAN COPY) – (continued)

LLCPAGHAV ($NS3_{1169-1177}$; SEQ ID NO:26),

SLMAFTAAV ($NS4_{1789-1797}$; SEQ ID NO:34), or

ILDSFDPLV ($NS5_{2252-2260}$; SEQ ID NO:42);

(d) combining the cytotoxic T cells separately with the matched and mismatched target cells; and

(e) measuring cytolysis.

89. **(Unchanged)** The method of claim 88, wherein the cytotoxic T cells are combined with HLA class I-matched lymphocytes.

90. **(Unchanged)** A pharmaceutical composition comprising a peptide that induces an hepatitis C virus (HCV)-specific response in cytotoxic T lymphocytes having a sequence that has no more than a total of two single amino acid substitutions, deletions or insertions at the corresponding positions as in a CTL epitope which is

ADLMGYIPLV ($Core_{131-140}$; SEQ ID NO:1),

LLALLSCLTV ($Core_{178-187}$; SEQ ID NO:2),

QLRRHIDLLV ($E1_{257-266}$; SEQ ID NO: 3),

KLVALGINAV ($NS3_{1406-1415}$; SEQ ID NO:28), or

LLFNILGGWV ($NS4_{1807-1816}$; SEQ ID NO:35) or

has no more than a total of one single amino acid substitution, deletion or insertion at the corresponding amino acid positions as in a CTL epitope which is

LLCPAGHAV ($NS3_{1169-1177}$; SEQ ID NO:26),

SLMAFTAAV ($NS4_{1789-1797}$; SEQ ID NO:34), or

ILDSFDPLV ($NS5_{2252-2260}$; SEQ ID NO:42), and

a pharmaceutically acceptable carrier.

APPENDIX A1: PENDING CLAIMS (CLEAN COPY) – (continued)

91. **(Unchanged)** The pharmaceutical composition of claim 90, wherein the peptide has less than 20 amino acids.

92. **(Unchanged)** A conjugate comprising

(a) a molecule, which comprises:

a polypeptide an having no more than a total of two single amino acid substitutions, deletions or insertions at the corresponding positions as in a CTL epitope which is

ADLMGYIPLV ($Core_{131-140}$; SEQ ID NO:1),

LLALLSCLTV ($Core_{178-187}$; SEQ ID NO:2),

QLRRHIDLLV ($E1_{257-266}$; SEQ ID NO: 3),

KLVALGINAV ($NS3_{1406-1415}$; SEQ ID NO:28), or

LLFNILGGWV ($NS4_{1807-1816}$; SEQ ID NO:35) or

has no more than a total of one single amino acid substitution, deletion or insertion at the corresponding amino acid positions as in a CTL epitope which is

LLCPAGHAV ($NS3_{1169-1177}$; SEQ ID NO:26),

SLMAFTAAV ($NS4_{1789-1797}$; SEQ ID NO:34), or

ILDSFDPLV ($NS5_{2252-2260}$; SEQ ID NO:42),; and

(b) a substance selected from the group consisting of a radiolabel, an enzyme, a fluorescent label, a solid matrix, a carrier and an additional molecule of (a).

93. **(Unchanged)** The conjugate of claim 92, wherein said carrier comprises an immunogenic lipid or protein.

APPENDIX A1: PENDING CLAIMS (CLEAN COPY) – (continued)

94. (**Unchanged**) A conjugate of claim 92 comprising two molecules, each comprising:

a polypeptide no more than a total of two single amino acid substitutions, deletions or insertions at the corresponding positions as in a CTL epitope which is

ADLMGYIPLV ($Core_{131-140}$; SEQ ID NO:1),

LLALLSCLTV ($Core_{178-187}$; SEQ ID NO:2),

QLRRHIDLLV ($E1_{257-266}$; SEQ ID NO: 3),

KLVALGINAV ($NS3_{1406-1415}$; SEQ ID NO:28), or

LLFNILGGWV ($NS4_{1807-1816}$; SEQ ID NO:35) or

has no more than a total of one single amino acid substitution, deletion or insertion at the corresponding amino acid positions as in a CTL epitope which is

LLCPAGHAV ($NS3_{1169-1177}$; SEQ ID NO:26),

SLMAFTAAV ($NS4_{1789-1797}$; SEQ ID NO:34), or

ILDSFDPLV ($NS5_{2252-2260}$; SEQ ID NO:42).

95. (**Unchanged**) The conjugate of claim 94, wherein at least one of said molecules comprises at least eight amino acids and less than 50 amino acids.

96. (**Unchanged**) The conjugate of claim 94, further comprising a T helper epitope.

97. (**Amended**) An isolated molecule comprising a polypeptide that induces an hepatitis C virus (HCV)-specific response in cytotoxic T lymphocytes having a sequence that has

(a) no more than a total of two single amino acid substitutions, deletions or insertions at the corresponding amino acid positions in a CTL epitope which is

LLALLSCLTV ($Core_{178-187}$; SEQ ID NO:2),

cont'd.

APPENDIX A1: PENDING CLAIMS (CLEAN COPY) – (continued)

QLRRHIDLLV ($E1_{257-266}$; SEQ ID NO:3),

KLVALGINAV ($NS3_{1406-1415}$; SEQ ID NO:28), or

LLFNILGGWV ($NS4_{1807-1816}$; SEQ ID NO:35), or

(b) has no more than one single amino acid substitution, deletion or insertion at the corresponding amino acid positions as in a CTL epitope which is

ADLMGYIPLV ($Core_{131-140}$; SEQ ID NO:1),

LLCPAGHAV ($NS3_{1169-1177}$; SEQ ID NO:26), or

SLMAFTAAV ($NS4_{1789-1797}$; SEQ ID NO:34),

wherein said polypeptide comprises at least eight amino acids and less than 50 amino acids, wherein said selected CTL epitope maintains an

`XaaLeuXaaXaaXaaXaaXaaXaaVal` or

`XaaLeuXaaXaaXaaXaaXaaXaaXaaVal` motif,

with the provisos that (a) when said selected CTL epitope is SLMAFTAAV ($NS4_{1789-1797}$; SEQ ID NO:34), then said polypeptide comprises from at least eight amino acids to less than 25 amino acids, and (b) when said selected CTL epitope is LLALLSCLTV ($Core_{178-187}$; SEQ ID NO:2) then said molecule comprises at most ten amino acids.

APPENDIX A2: CHANGES TO CLAIMS (VERSION WITH MARKINGS TO SHOW CHANGES MADE, I.E., REDLINE)

67. (**Amended**) An isolated molecule comprising a polypeptide that induces an hepatitis C virus (HCV)-specific response in cytotoxic T lymphocytes having a sequence that **[**~~has~~**]**

(a) has no more than a total of two single amino acid substitutions, deletions or insertions at the corresponding amino acid positions in a CTL epitope which is

LLALLSCLTV ($Core_{178-187}$; SEQ ID NO:2),

QLRRHIDLLV ($E1_{257-266}$; SEQ ID NO:3),

KLVALGINAV ($NS3_{1406-1415}$; SEQ ID NO:28), or

LLFNILGGWV ($NS4_{1807-1816}$; SEQ ID NO:35), or

(b) has no more than one single amino acid substitution, deletion or insertion at the corresponding amino acid positions as in a CTL epitope which is

ADLMGYIPLV ($Core_{131-140}$; SEQ ID NO:1),

LLCPAGHAV ($NS3_{1169-1177}$; SEQ ID NO:26), or

SLMAFTAAV ($NS4_{1789-1797}$; SEQ ID NO:34), **[**~~or~~

~~ILDSFDPLV ($NS5_{2252-2260}$; SEQ ID NO:42),~~**]**

wherein said molecule comprises at least eight amino acids and less than 50 amino acids, with the provisos that (i) when said selected CTL epitope is SLMAFTAAV ($NS4_{1789-1797}$; SEQ ID NO:34), then said molecule comprises from at least eight amino acids to less than 25 amino acids, or (ii) when said selected CTL epitope is LLALLSCLTV ($Core_{178-187}$; SEQ ID NO:2) then said molecule comprises at most ten amino acids **[**~~, and (iii) when said selected CTL epitope is ILDSFDPLV ($NS5_{2252-2260}$; SEQ ID NO:42) then said molecule comprises at most nine amino acids~~**]**.

97. (**Amended**) An isolated molecule comprising a polypeptide that induces an hepatitis C virus (HCV)-specific response in cytotoxic T lymphocytes having a sequence that has

APPENDIX A2: CHANGES TO CLAIMS (REDLINE) – (continued)

(a) no more than a total of two single amino acid substitutions, deletions or insertions at the corresponding amino acid positions in a CTL epitope which is

LLALLSCLTV ($Core_{178-187}$; SEQ ID NO:2),

QLRRHIDLLV ($E1_{257-266}$; SEQ ID NO:3),

KLVALGINAV ($NS3_{1406-1415}$; SEQ ID NO:28), or

LLFNILGGWV ($NS4_{1807-1816}$; SEQ ID NO:35), or

(b) has no more than one single amino acid substitution, deletion or insertion at the corresponding amino acid positions as in a CTL epitope which is

ADLMGYIPLV ($Core_{131-140}$; SEQ ID NO:1),

LLCPAGHAV ($NS3_{1169-1177}$; SEQ ID NO:26), or

SLMAFTAAV ($NS4_{1789-1797}$; SEQ ID NO:34), [~~or~~ ~~ILDSFDPLV ($NS5_{2252-2260}$; SEQ ID NO:42),~~]

wherein said polypeptide comprises at least eight amino acids and less than 50 amino acids, wherein said selected CTL epitope maintains an

`XaaLeuXaaXaaXaaXaaXaaXaaVal` or

`XaaLeuXaaXaaXaaXaaXaaXaaXaaVal` motif,

with the provisos that (a) when said selected CTL epitope is SLMAFTAAV ($NS4_{1789-1797}$; SEQ ID NO:34), then said polypeptide comprises from at least eight amino acids to less than 25 amino acids, and (b) when said selected CTL epitope is LLALLSCLTV ($Core_{178-187}$; SEQ ID NO:2) then said molecule comprises at most ten amino acids [~~, and (c) when said selected CTL epitope is ILDSFDPLV ($NS5_{2252-2260}$; SEQ ID NO:42), then said molecule comprises at most nine amino acids~~].